

LADTAG Progress 2010 and Plans for 2011

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Overview

- Pilot ITI Studies: lavage & histopath
- Core ITI Studies: lavage & histopath
- Macrophage activation studies: lavage
- Inhalation plan: 2 concentrations + control
- Grinding dust/size fractionation
- Dissolution studies
- Cellular studies
- Ocular studies
- Dermal studies



ITI Studies

- Pilot studies at NIOSH for dose ranging
- Core studies at NIOSH with 7 and 30-day assessment of lavage fluid/blood
- Benchmark dose modeling of useful endpoints
- Core studies with 4 w and 13 w harvesting for histopathology



Inhalation plan

- One week inhalation study of lunar dust simulant to demonstrate nose-only chamber performance
- Four-week study of authentic lunar dust ground to a respirable size
- Exposures
 - Control air
 - 25 mg/m³
 - 75 mg/m³
- Endpoints taken as follows
 - Lavage fluid
 - Histopathology



Supporting Studies

- Progress on grinding and size separation
- Dissolution studies of metals from dust at various pH levels with morphological changes
- Cellular studies of simulant and readiness for use of authentic lunar dust
- Ocular studies-in vitro results and in vivo plan
- Dermal studies-comments and progress on manuscript



Provisional PEL for Moon Dusts

- Based only on 7 and 28 day post-dosing lavage fluid data and blood markers
- Five dusts were used to dose rats at three concentrations
- Used EPA benchmark software to estimate a BMD10 for each dust
- Compared BMD10s to known PELs to estimate PEL of dusts with unknown PELs



Provisional PELs from Lavage and Blood Data

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Pathway

- For each endpoint and all 5 dusts, inspect dose-response curves for effect
- Determine if all curves for a given endpoint will produce a BMD10 (TiO₂ may not)
- Fit the best of the 5 EPA benchmark curves to the dose response curve for each dust and endpoint
- Compare the BMD10s and PELs on a log-log basis to estimate PPELs from each endpoint

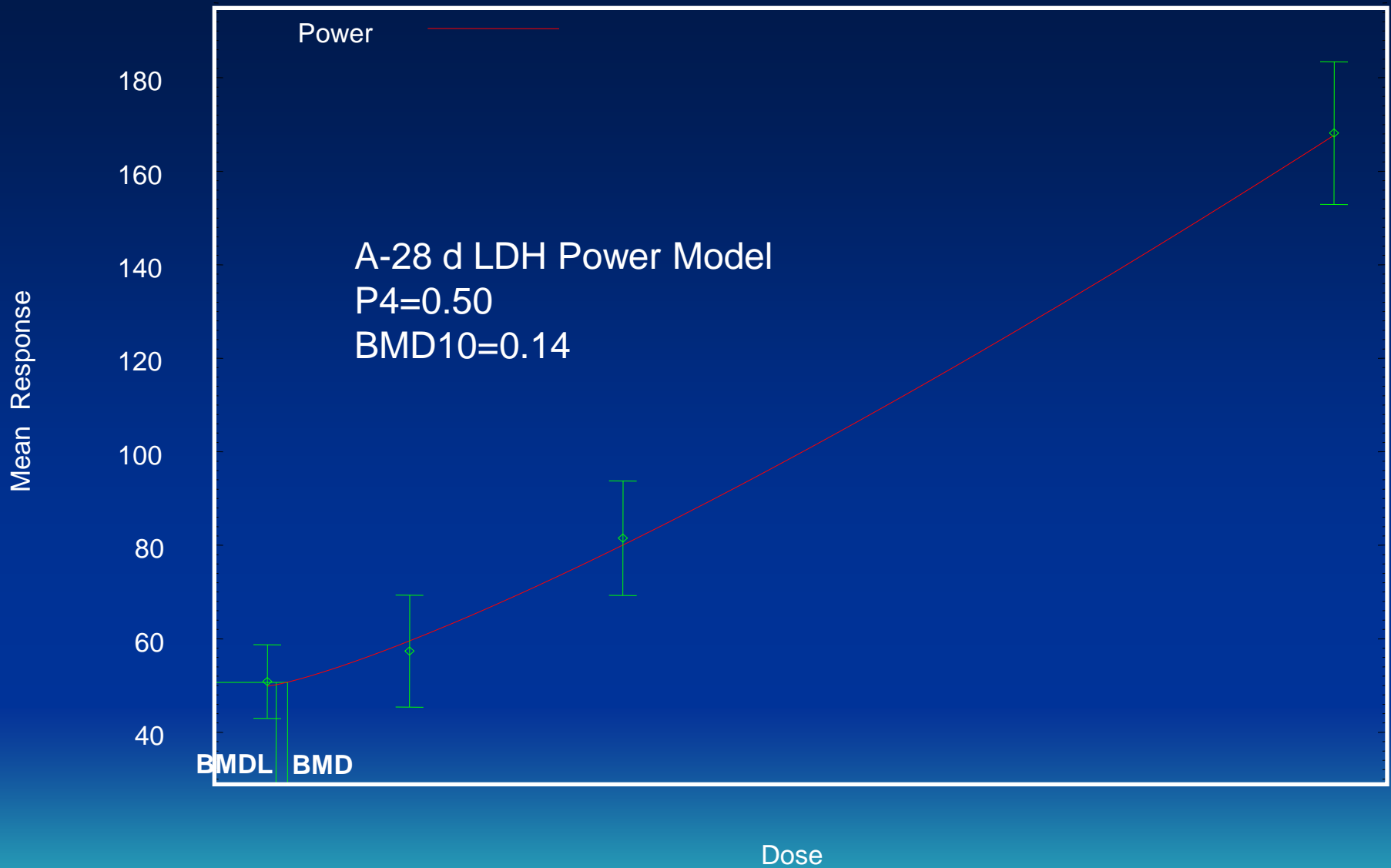


Inspect Dose Response Profiles

- No chance
- Maybe useful
- Likely to be useful

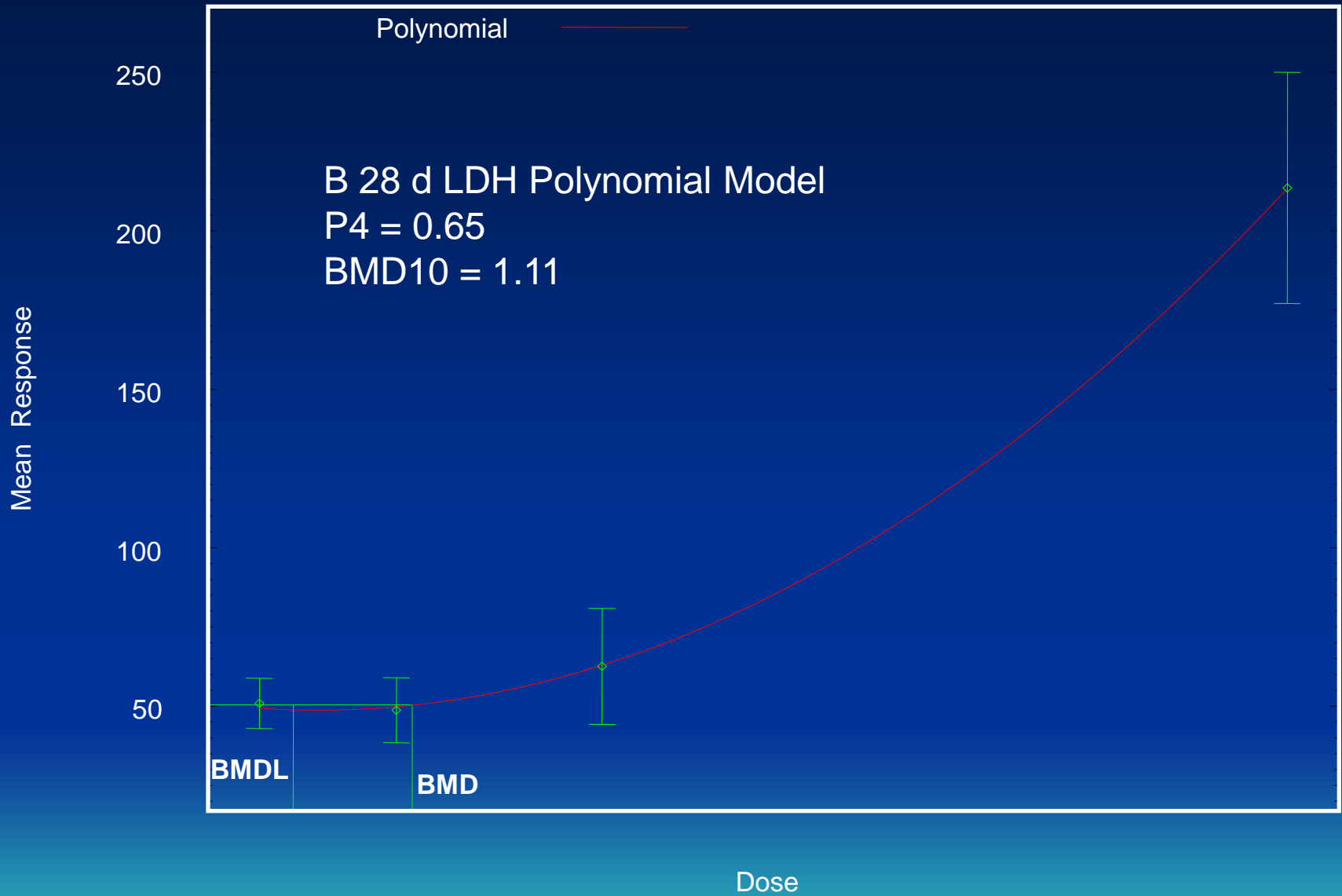


Power Model with 0.95 Confidence Level



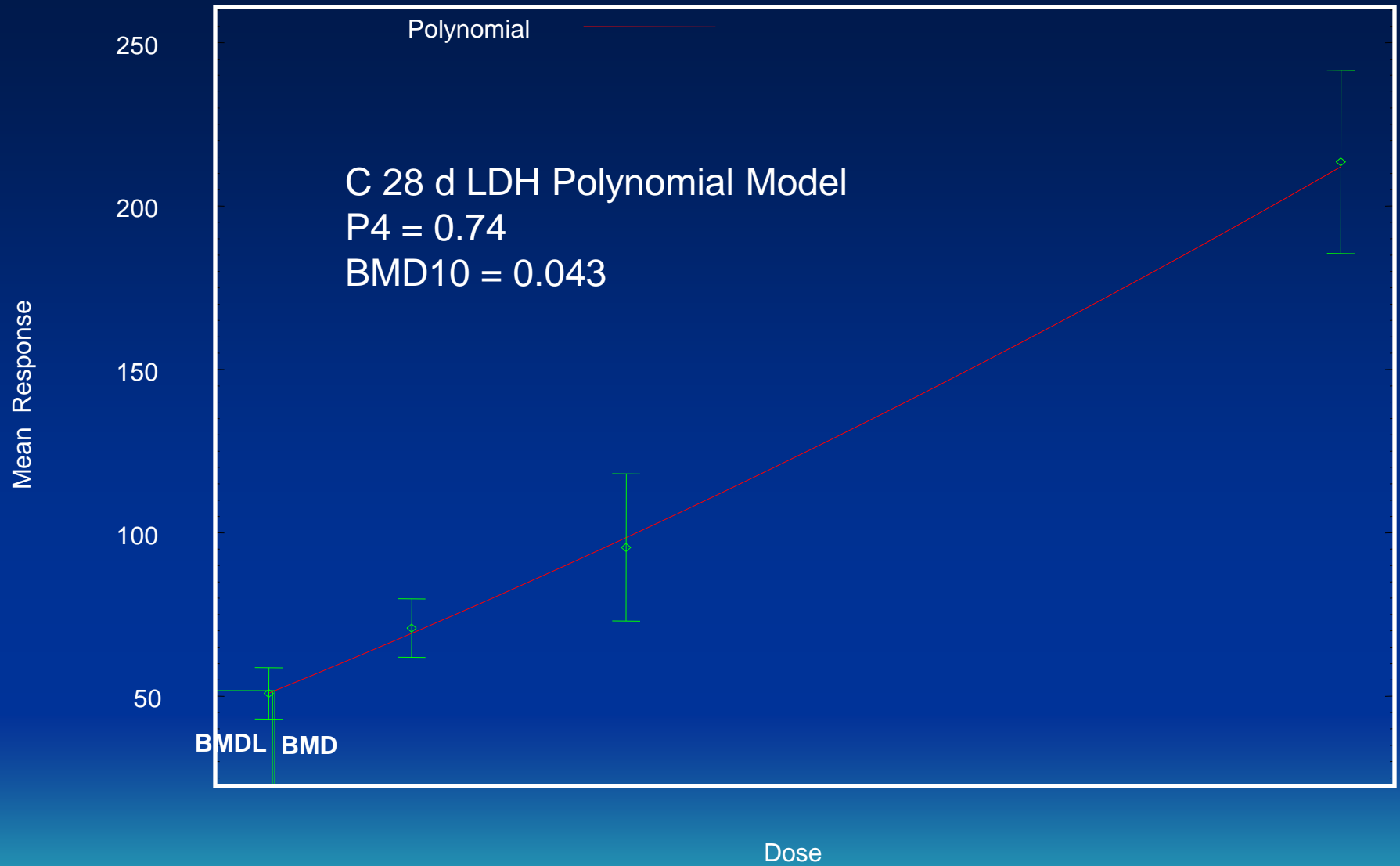
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Polynomial Model with 0.95 Confidence Level



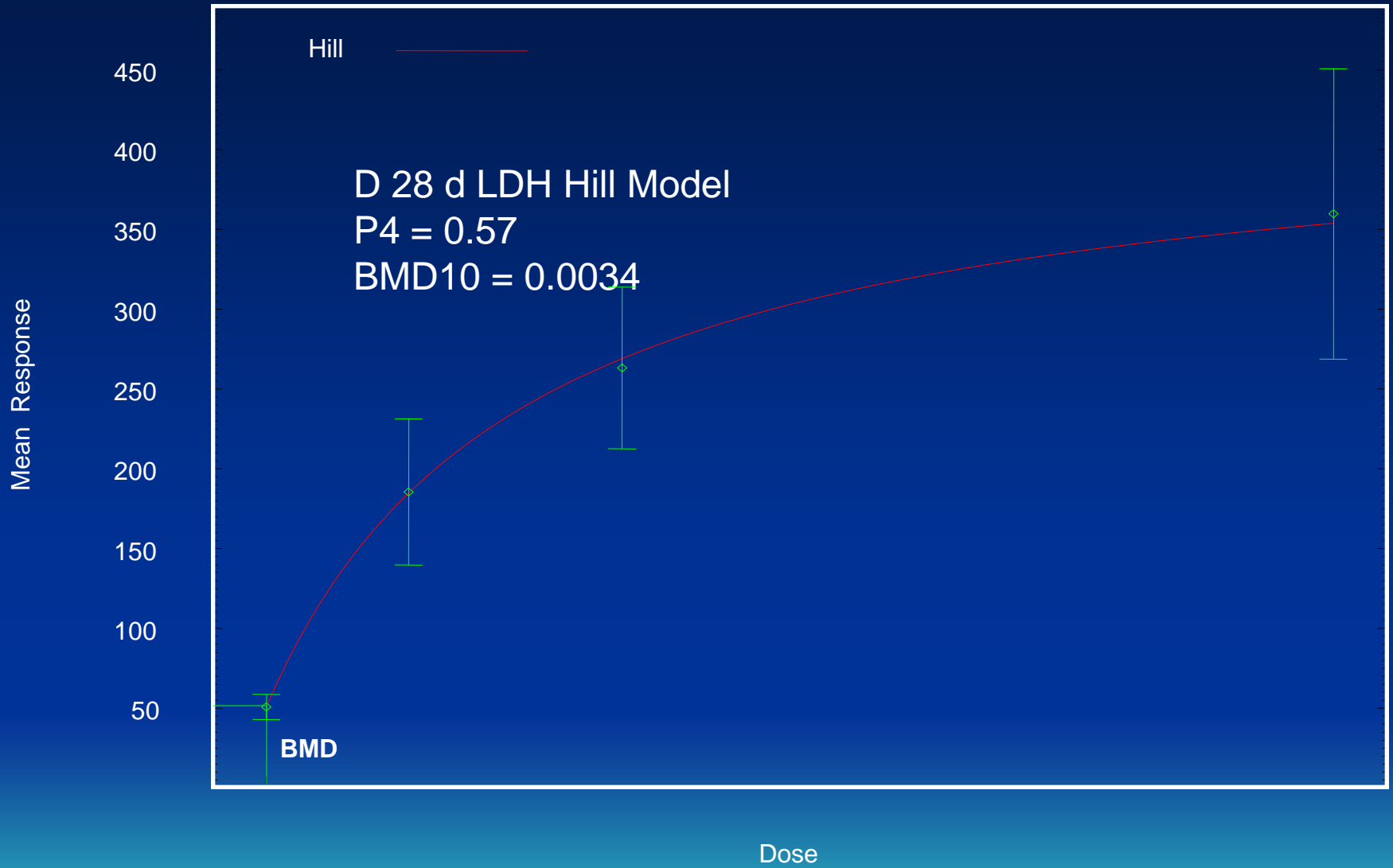
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Polynomial Model with 0.95 Confidence Level



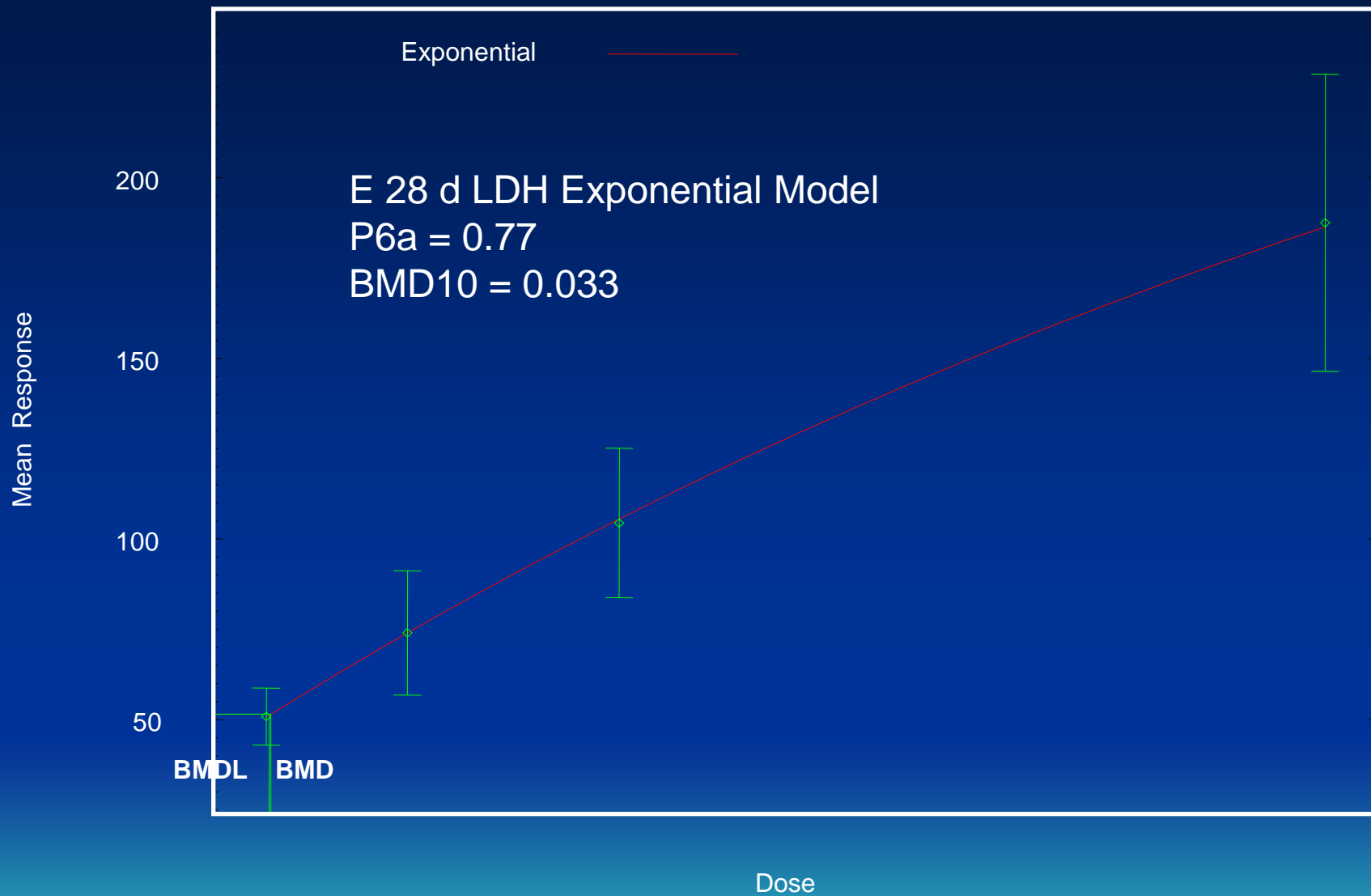
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Hill Model



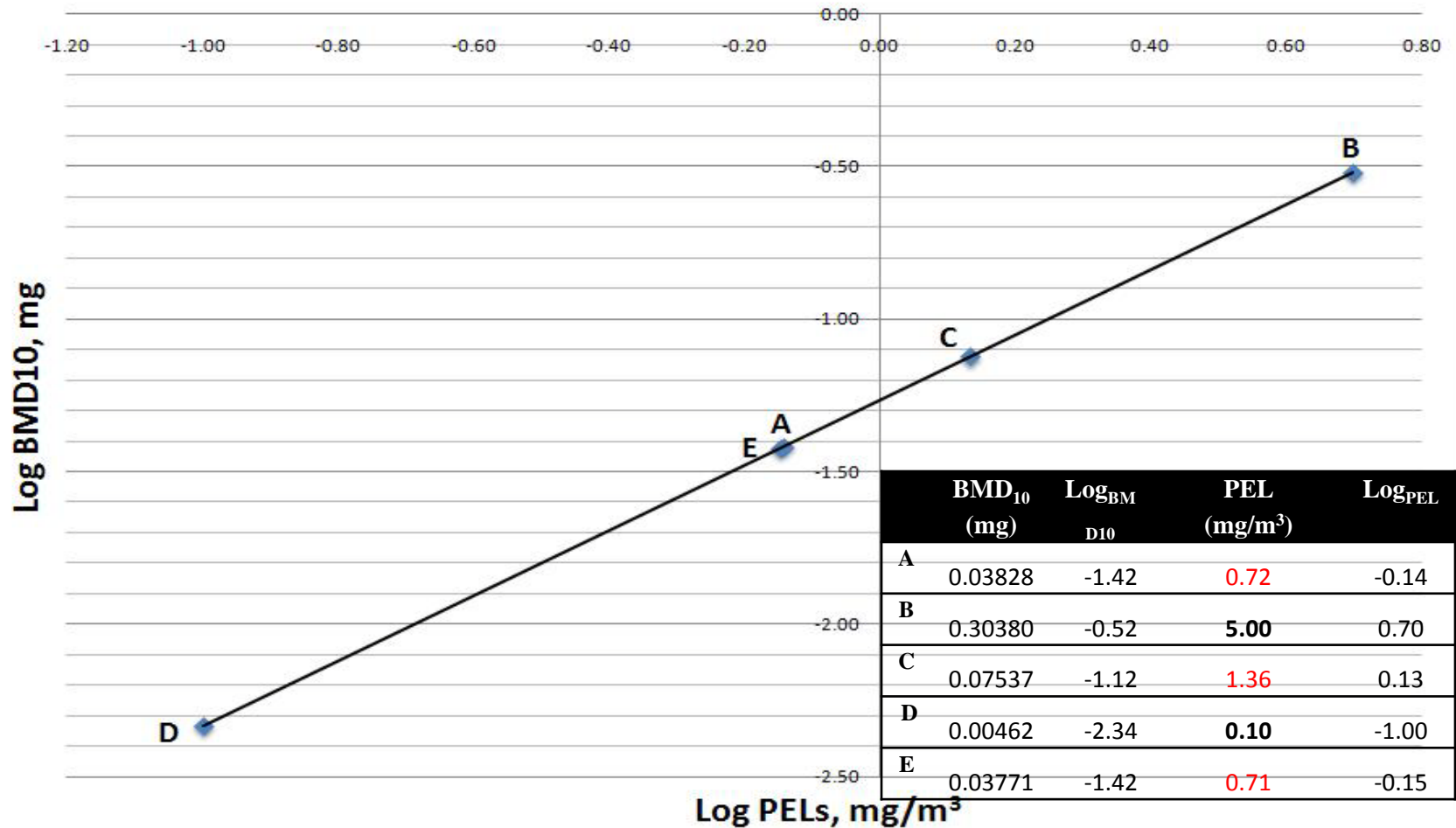
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Exponential Model 4 with 0.95 Confidence Level

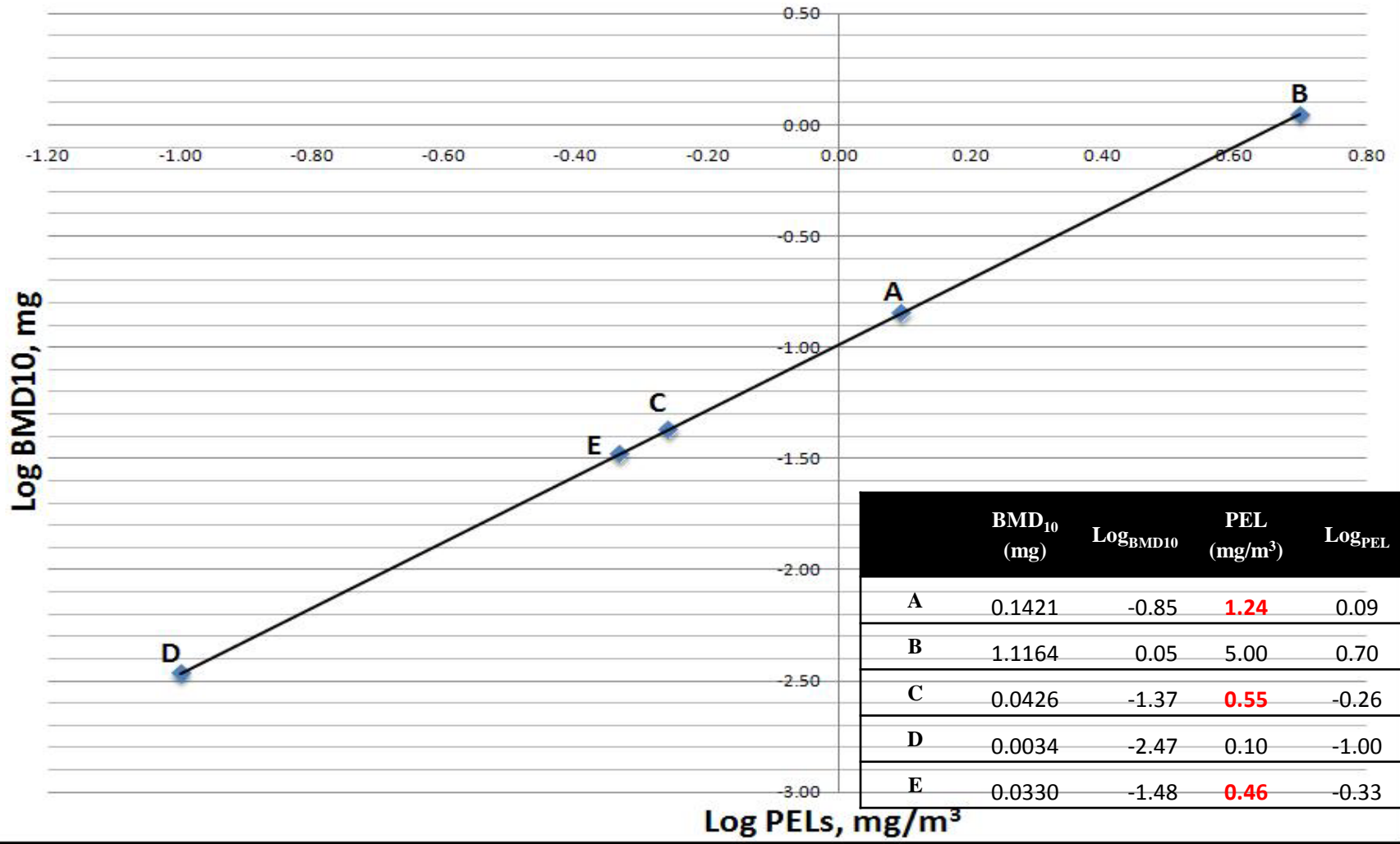


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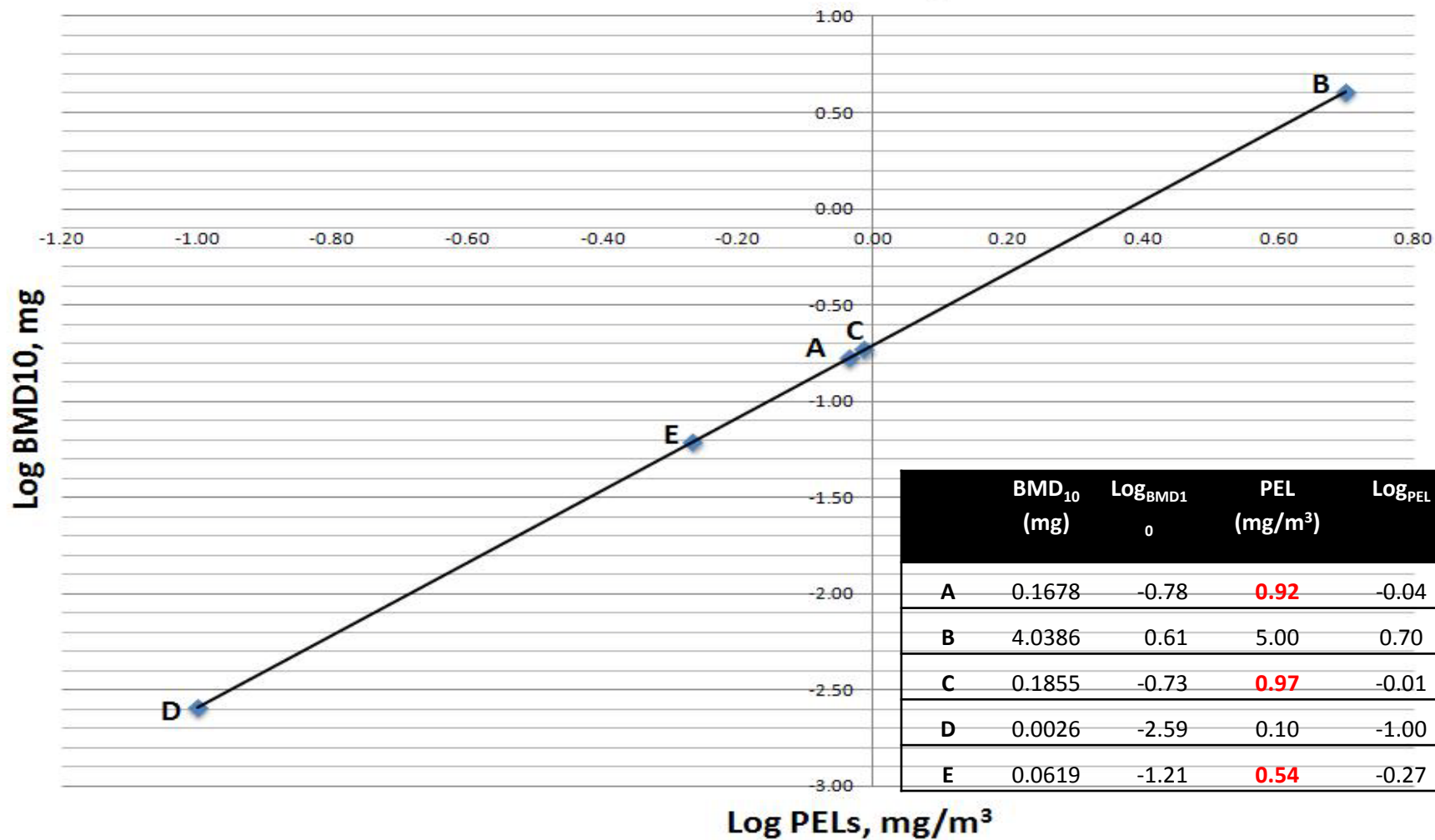
Lactate Dehydrogenase 7 Day Mark



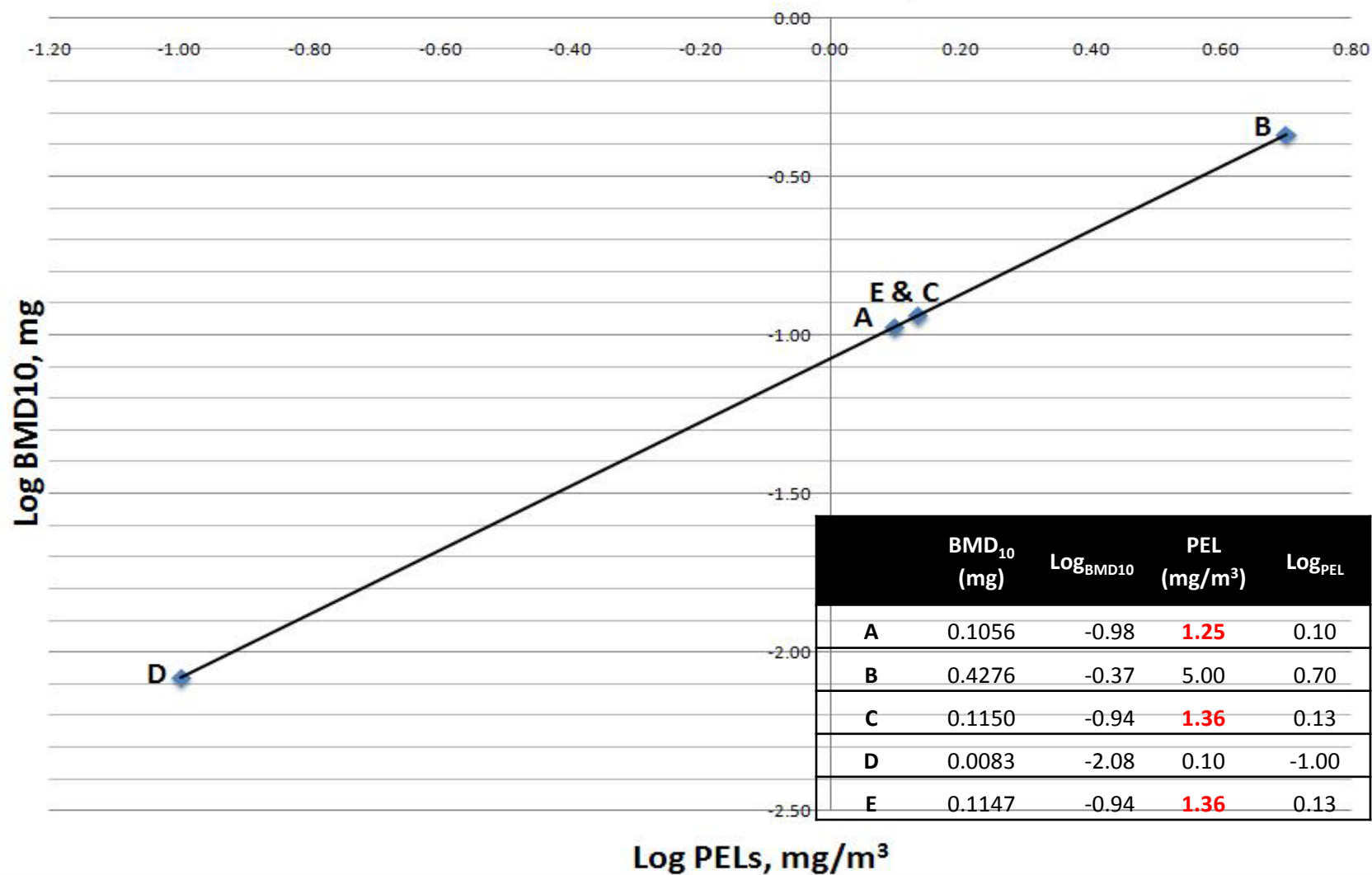
Lactate Dehydrogenase 28 Day Mark



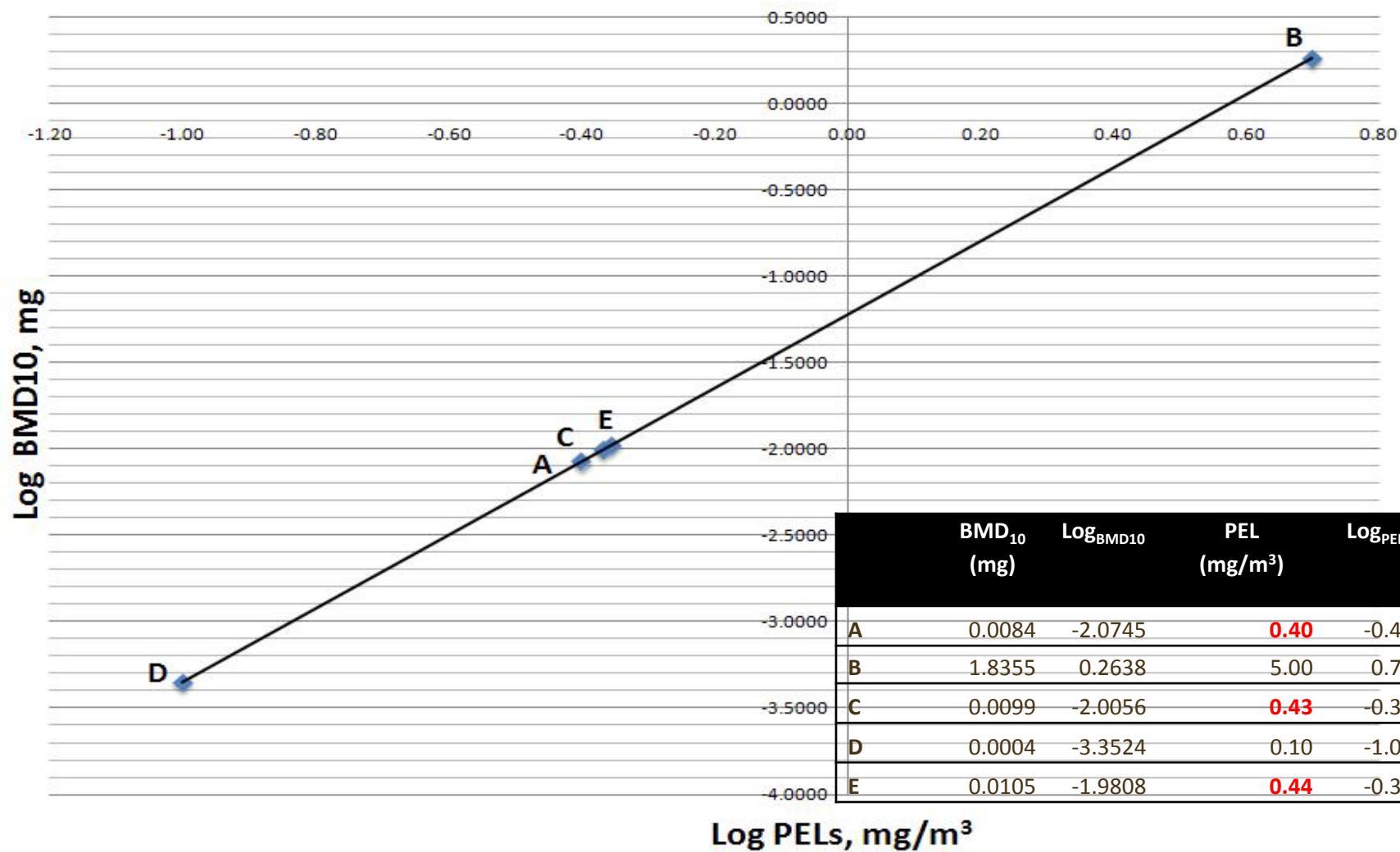
Total Cell Count 7 Day Mark



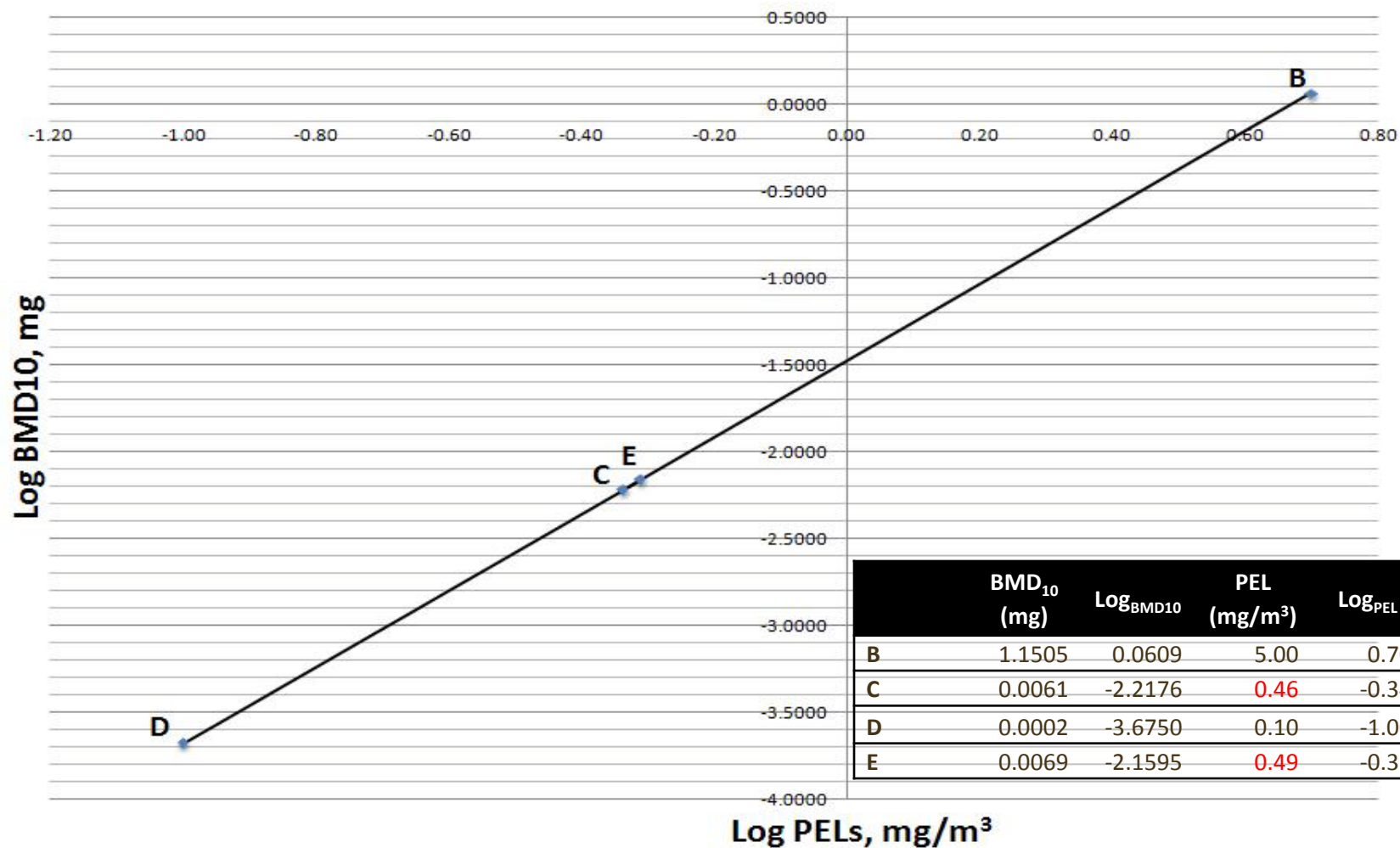
Total Cell Count 28 Day Mark



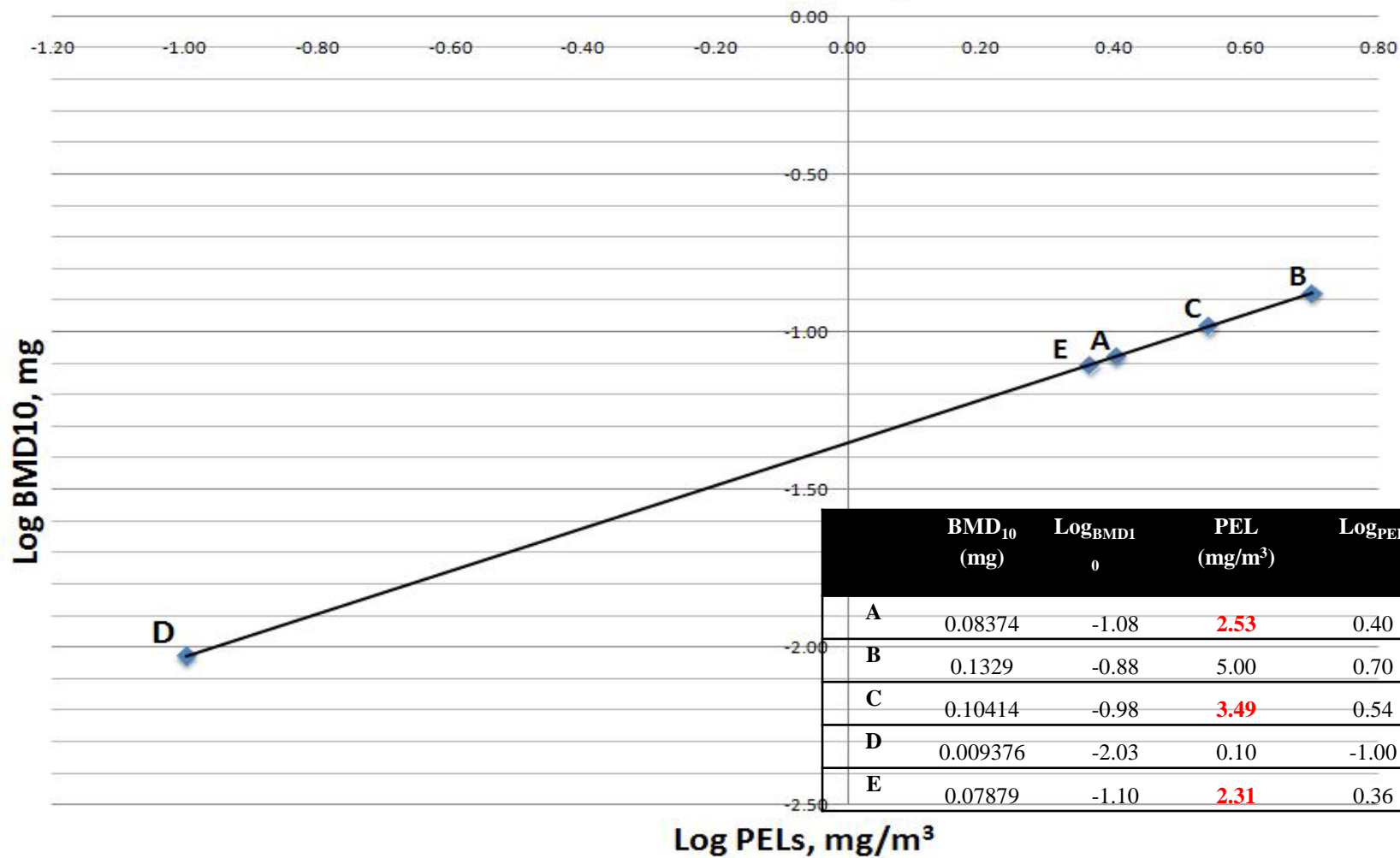
% Neutrophil Cell Differential 7 Day Mark



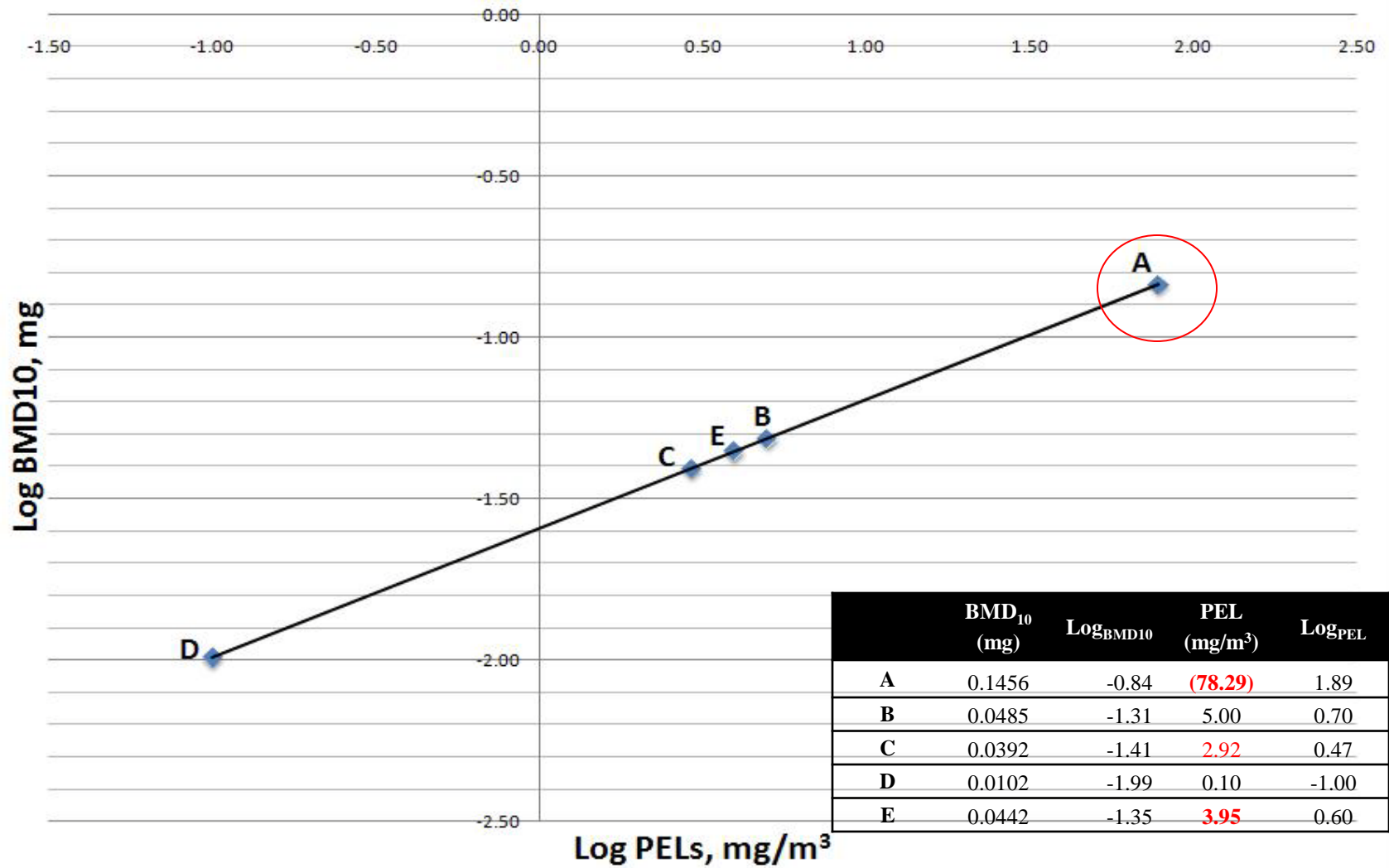
% Neutrophil Cell Differential 28 Day Mark



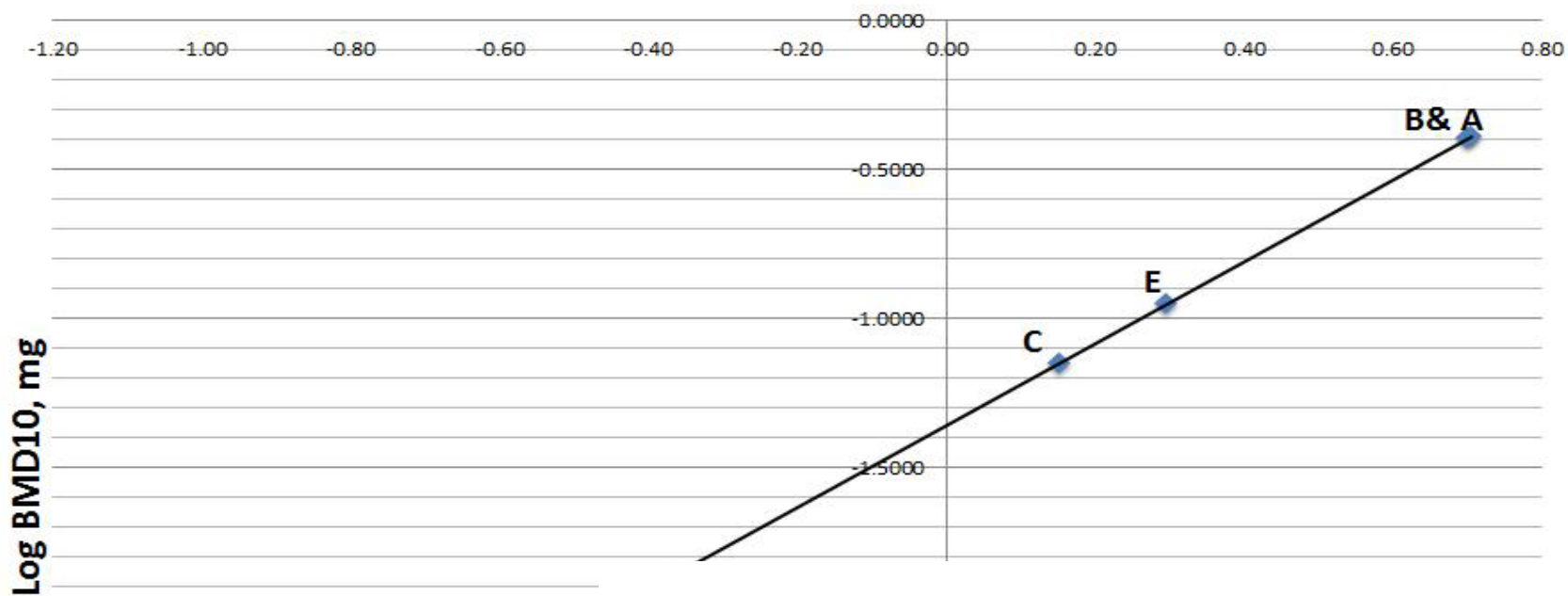
Total Protein 7 Day Mark



Total Protein 28 Day Mark

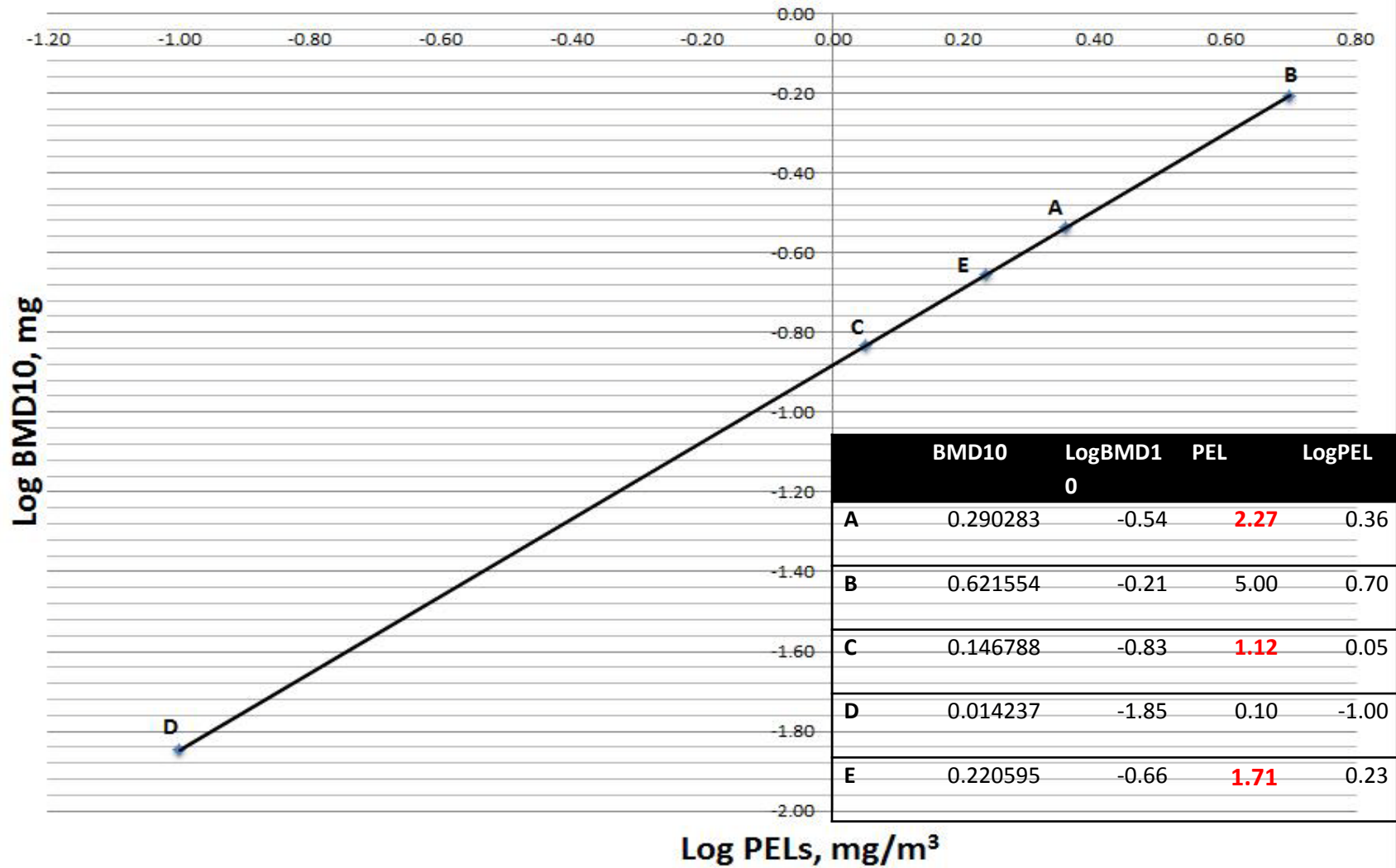


% Blood Neutrophil Level 7 Day Mark

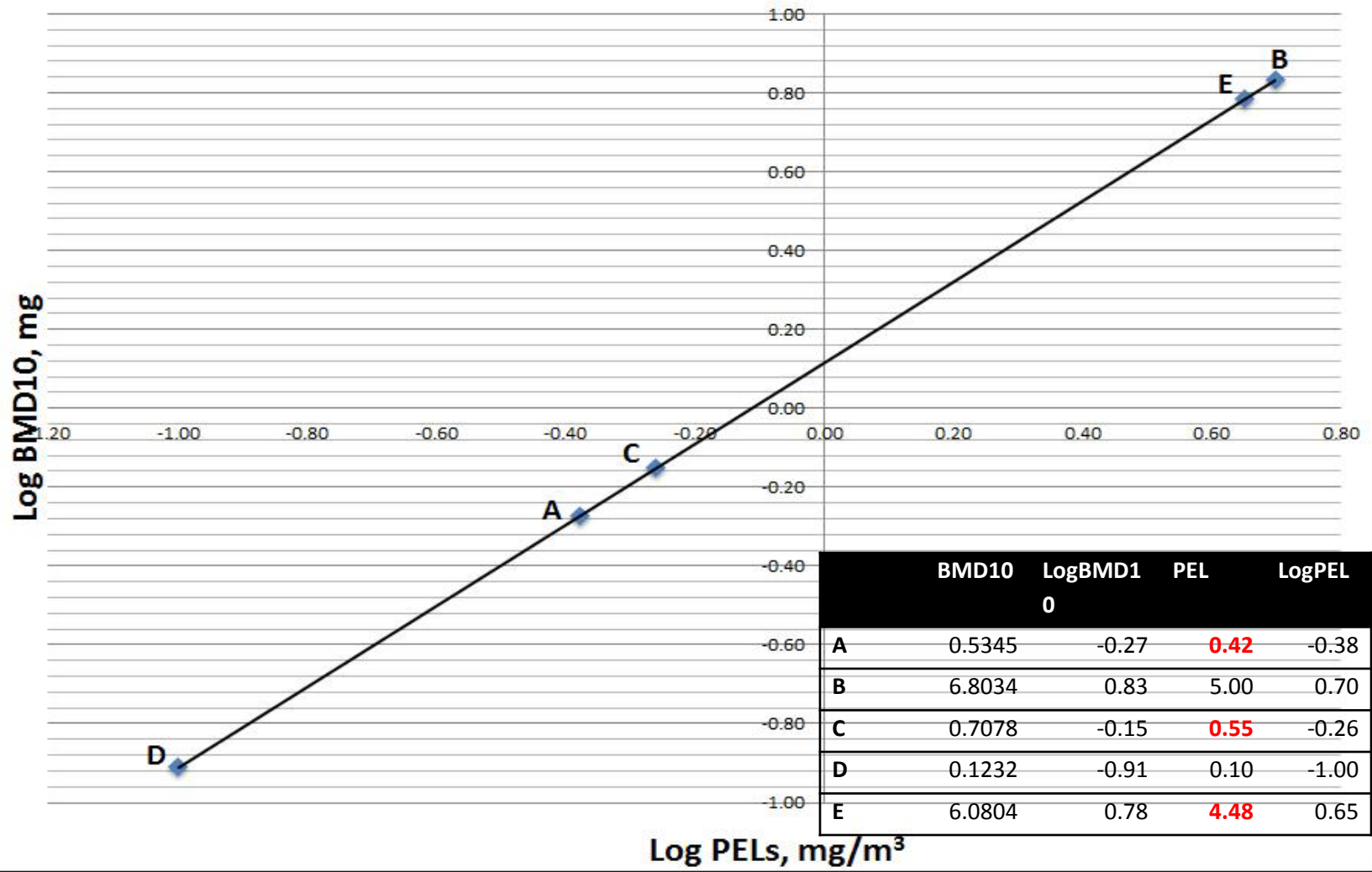


	BMD ₁₀	Log _{BMD10}	PEL	log PEL
A	0.4078	-0.3895	5.06	0.70
B	0.4010	-0.3969	5.00	0.70
C	0.0709	-1.1494	1.41	0.15
D	0.0019	-2.7266	0.10	-1.00
E	0.1122	-0.9500	1.97	0.30

AST Level 28 Day Mark



MCP-1 Levels 7 Day Mark



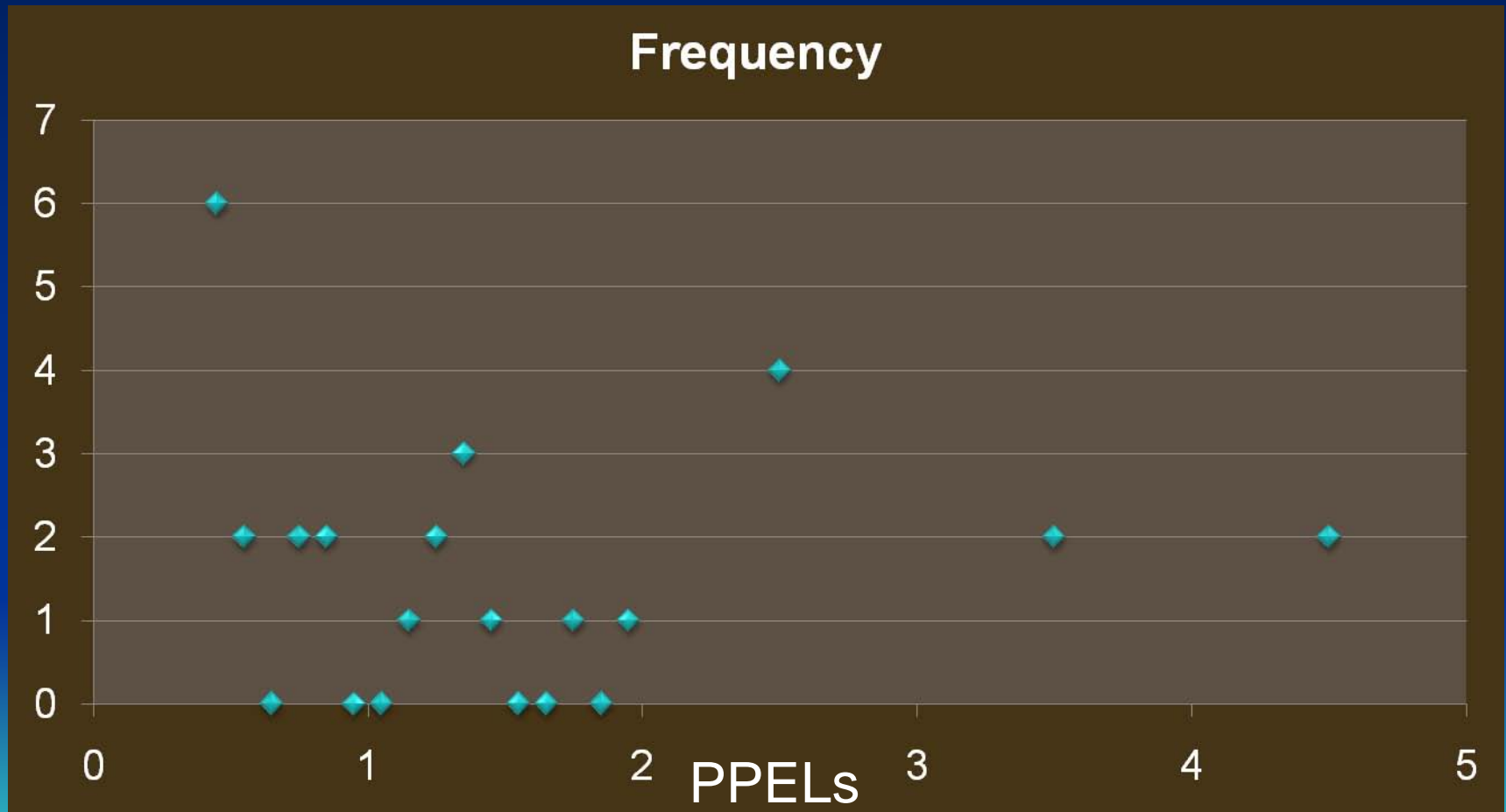
Test for Similarity of PPEs

- Wilcoxon Rank Sum Test

Comparison		Comparison		Comparison	
A (9)	95	A (9)	121	C (11)	122
C(11)	115	E (11)	116	E (11)	132



Array of PPELs



Proposed PPEL

- PELs for Quartz and TiO₂ are for lifetime intermittent exposures
- PPEL for moon dust applies for 6 months of intermittent exposure
- 0.4 mg/m³ would be very conservative
- 1.0 mg/m³ would be more defensible

